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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 10/03/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/599,452

Applicant(s)

BLOOM ET AL.

Examiner

David Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-129 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-129 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *attachment*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 20, 2002 has been entered.

New claims 103-129 have been added. Claims 42-129 are pending in the instant application.

The rejection of claims 42-102 under 35 U.S.C. 112, second paragraph has been withdrawn in view of the amendments to the claims and the remarks presented by Applicant in the reply filed on May 1, 2002.

Claim Objections

Claim 42, 50, 97-102 and 127-129 are objected to because of the following informalities: Claims 42, 97-102 and 127-129 should begin with an article. Claim 50 recites the term "endogenous vectors"; however, it appears that the term should read "endogenous plasmids". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43, 49, 50, 59, 60, 65, 70, 71, 93 and 99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant indicates the use of strain C as a limitation of these claims, but has not adequately described the strain in the specification so that the skilled artisan would know how to use the strain, or even if he possessed the strain. Applicant has not indicated the nature of strain C in terms of how to make the strain, what the genotype of the strain is, or where the strain is available in terms of a deposit number. Therefore, these claims fail to meet the written description requirement.

Claims 42-129 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims cells that grow at least 5% faster than a reference microorganism, and various uses of these cells (transformation, polypeptide production, etc.). Applicant provides a written description on only the use of *E. coli* strain W to generate these cells and perform this method. Applicant's claims read on a genus of strains capable of generating these cells and performing this method.

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The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicant was in possession of the claimed genus. In the instant case, applicant's claims encompass all strains that have growth rates that are at least 5% greater than those of the reference microorganism. However, applicant has provided a written description and reduction to practice of examples of only one particular strain (ATCC 9637) and genetic modifications of said strain. It is apparent that there are numerous bacterial strains in existence, some of which may grow at least 5% greater than those of the reference microorganism (with and without the removal of endogenous plasmids). Applicant claims the components of the cells by function only, without any disclosed knowledge of a sufficient number of strains that are capable of meeting the "growth rates that are at least 5% greater than those of the reference microorganism" limitation. As applicant has only disclosed a written description for the indicated strain (ATCC 9637) and derivatives generated from the strain, and not for a representative number of strains through specific identifying characteristics, they have not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus. Applicant is duly reminded that the limitation of "having all endogenous plasmids removed from a strain" is not a limitation in all of the claims as stated in the instant application, and therefore cannot represent a written description of a specific identifying characteristic as indicated above. Furthermore, in the event applicant amends the claims to include this limitation, it is still lacking

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as a specific identifying characteristic because strains can be envisioned that lack endogenous plasmids but still grow slower than the indicated reference microorganisms (such as slow growth mutants of the reference microorganisms).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 51 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51 recites the limitation "recombinant vector". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 75, 82-85, 88-90 and 118-123 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention. See attached information sheet obtained from ATCC concerning *E. coli* strain W (ATCC 9637).

Claims 75 and 85 are independent claims referring to a kit and a composition, respectively, containing an *E. coli* strain with at least 5% greater growth rate than reference

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organisms. Claims 82-83 and 88-89 are corresponding dependent claims where the limitations are that the reference organisms indicated in the independent claims are considered individually. Claims 84 and 90 are corresponding dependent claims reciting a range limitation for the growth rate of the claimed strain. Claims 118-120 and 121-123 are corresponding dependent claims where the growth rates are claimed more narrowly. It is duly pointed out to applicant that the aforementioned claims do not contain a step involving the removal of endogenous plasmids. Therefore, each of these claims is anticipated by the ATCC 9637 strain, as indicated by Table 4 (page 40) of the specification and by applicant's own admissions in the specification that this strain grows significantly faster than the reference strains mentioned (page 2, lines 16-20). Since this strain has been commercially available since December 6, 1944 according to ATCC, this is a 35 U.S.C. 102(b) rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42, 43, 45-47 and 103-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's admissions concerning *E. coli* strain W (ATCC 9637; see 102(b) rejection for locations of admissions) in view of Trevors (*FEMS Microbiol. Rev.* **32**:149-157 (1986); henceforth Trevors).

Briefly, applicant's invention is an isolated bacterial strain exhibiting at least a 5% increased growth rate with respect to reference *E. coli* strains MM294, DH5 α and DH10B. In some embodiments, the isolated strains are cured of endogenous plasmids. Limitations of the invention include the use of specific isolated *E. coli* strains to be compared to the reference strains. In particular, applicant explicitly states *E. coli* strain W (ATCC 9637) as one of the isolated strains to be compared to the reference strains. The isolated strains can be used to make competent cells for transformation, in the form of kits and compositions used for transformations, and for the production of polypeptides as recited in limitations of the claims.

Concerning *E. coli* strain W, it is known that this strain exhibits an increased growth rate with respect to the reference strains of the instant application, which applicant clearly indicates on page 2, lines 16-20 of the instant application. As per Table 4 of the specification of the instant application (page 40), *E. coli* strain W grows at a rate that is 100% faster than DH5 α , thus it is an inherent property of the strain to grow at least 5%, 25%, 50% or 100% faster than the reference strains. However, this strain contains endogenous plasmids and is RecA⁺ (relevant to claim 44 only), so the strain itself does not anticipate all of the claims.

Trevors teaches the use of plasmid curing agents to remove plasmids from bacteria (see page 150, Table 1) and the desirability of curing plasmids from bacteria (see page 149, paragraphs 2-3). Trevors modifies *E. coli* strain W by removing endogenous plasmids from the strain. Therefore, applying the teachings of Trevors to *E. coli* strain W teaches the inventive step of claims 42, 43, 45-47 and 103-105 in the instant application. The ordinary skilled artisan would have been motivated to apply the teachings of Trevors to *E. coli* strain W in order to obtain a strain that was unhindered in growth by the replication of extra DNA (plasmids), and which did not contain plasmids that could potentially interfere with biotechnological applications (cloning/plasmid recovery, etc.). It would have been obvious to apply Trevors to *E. coli* strain W because the method of Trevors is directed to a bacterial strain harboring plasmids, which *E. coli* strain W represents. Given the teachings of the stated prior art and the level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

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Claims 48, 49, 51, 55-57, 69, 70, 72-74, 76-81, 86, 87, 91, 93-97, 99-102, 106-108, 115-117 and 124-129 are rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's admissions concerning *E. coli* strain W in view of Jessee, *et al.* (US Patent No. 4,981,797; henceforth Jessee). It is duly pointed out to applicant that aforementioned claims do not contain a step involving the removal of endogenous plasmids.

Applicant's invention is as described above.

E. coli strain W is as described above. However, the strain itself does not inherently teach using the cells to make competent cells, the resulting cells/compositions/kits, or the use of the competent cells for transformation/cloning.

Jessee teaches a procedure for making competent bacterial cells (therefore compositions and kits containing these cells) (see column 2, lines 1-35), and the use of these cells in transformation and cloning procedures (see column 2, lines 39-59). Inherent properties of these procedures are the use of cloning techniques (use of recombinases, restriction enzymes, ligases, DNA fragments, vectors, etc.) and that the cells are stored in competence buffer. Therefore the limitations recited in the claims of the instant application concerning the inclusion of these items in a kit with the cells cannot overcome the prior art due to an inherent need for one or more of these reagents during the cloning process. *E. coli* strain W is modified by Jessee by using the cells to make competent cells for transformation/cloning, therefore describing the inventive steps as set forth in claims 48, 49, 51, 55-57, 69, 70, 72-74, 76-81, 86, 87, 91, 93-97, 99-102, 106-108, 115-117 and 124-129 of the instant application. The ordinary skilled artisan would have been motivated to combine these teachings in order to obtain competent cells that could grow faster when used in cloning reactions. It would have been obvious to combine these teachings because

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the method described by Jessee is for use with bacterial cells, which the cells of *E. coli* strain W represent. Given the teachings of the stated prior art and the level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 50, 64-68, 71, 92, 98 and 112-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's admissions concerning *E. coli* strain W in view of Trevors, and in further view of Jessee.

Applicant's invention is as described above.

E. coli strain W in view of Trevors teaches an *E. coli* strain lacking plasmids which can grow 100% faster than a reference strain DH5 α . *E. coli* strain W in view of Trevors does not teach using the resulting strain to make competent cells, the resulting cells/compositions/kits, or the use of the competent cells for transformation/cloning.

Jessee teaches a procedure for making competent bacterial cells, as described above.

E. coli strain W in view of Trevors is modified by Jessee by using the cells to make competent cells for transformation/cloning, therefore describing the inventive steps as set forth in claims 50, 64-68, 71, 92, 98 and 112-114 of the instant application. The ordinary skilled artisan would have been motivated to combine these teachings in order to obtain competent cells lacking endogenous plasmids that could interfere with cloning/transformation reactions (i.e., plasmid recovery). It would have been obvious to combine these teachings because the method described by Jessee is for use with bacterial cells, which the cells of *E. coli* strain W in view of Trevors represent. Given the teachings of the stated prior art and the level of skill of the ordinary skilled

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artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 58, 59, 61-63 and 109-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's admissions concerning *E. coli* strain W in view of Jessee, in further view of Nathan, *et al.* (US Patent No. 5,914,390; henceforth Nathan). It is duly pointed out to applicant that aforementioned claims do not contain a step involving the removal of endogenous plasmids.

Applicant's invention is as described above.

E. coli strain W in view of Jessee describes competent cells as outlined above. However, they do not teach the use of these strains for the production of recombinant polypeptides.

Nathan teaches a method for increased recombinant polypeptide production using *E. coli* as a recombinant host cell (see column 3, lines 1-20). *E. coli* strain W in view of Jessee is modified by Nathan to include the production of recombinant polypeptides as a use for the cells, therefore teaching the inventive step of claims 58, 59, 61-63 and 109-111 of the instant application. The ordinary skilled artisan would have been motivated to combine the teachings in order to produce polypeptides in a more timely fashion, owing to the faster growing properties of *E. coli* strain W. It would have been obvious to combine these teachings because the method of Nathan is designed for use with bacterial cells, which are represented by *E. coli* strain W. Given the teachings of the stated prior art and the level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's admissions concerning *E. coli* strain W in view of Trevors, and in further view of Jessee, and in further view of Nathan.

Applicant's invention is as described above.

E. coli strain W in view of Trevors, and in further view of Jessee describes competent cells as outlined above. However, they do not teach the use of these strains for the production of recombinant polypeptides.

Nathan teaches a method for increased recombinant polypeptide production as indicated above. *E. coli* strain W in view of Trevors, and in further view of Jessee is modified by Nathan to include the production of recombinant polypeptides as a use for the cells, therefore teaching the inventive step of claim 60 of the instant application. The ordinary skilled artisan would have been motivated to combine the teachings in order to produce polypeptides in strain lacking endogenous plasmids, such as those described by Trevors modified *E. coli* strain W, so that the endogenous plasmids would not interfere with maintenance of the plasmid of interest. It would have been obvious to combine these teachings because the method of Nathan is designed for use with bacterial cells, which are represented by the Trevors modified *E. coli* strain W. Given the teachings of the stated prior art and the level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
September 27, 2002

DAVID GUZO
PRIMARY EXAMINER
David Guzo